Diagnosis and management of depression in adolescents

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Depression is common, a leading cause of disability and a major contributor to the overall global burden of disease.[1] Although more than 40% of people with depression experience onset before adulthood, depression remains undetected in many adolescents in Canada, and most are untreated.[2–4] Clinicians consistently report a lack of confidence in their ability to care for adolescents with depression.[5] We review the diagnosis and management of depression in adolescents, drawing on available evidence and recommendations from international guidelines, as outlined in Box 1.

Key points

- Depression is common among adolescents in Canada and has the potential to negatively affect long-term function and quality of life; despite this, in most affected adolescents depression remains undetected and untreated.
- Management requires a multimodal approach, including risk assessment, psychoeducation, psychotherapeutic and pharmacologic treatment, and interventions to address contributing factors.
- Support from child and adolescent psychiatrists may be required in the case of diagnostic uncertainty and complex presentations, as well as for patients who do not respond to first-line treatments.

Box 1: Evidence used in this review

We conducted a targeted search of MEDLINE, PubMed and PsycINFO using keywords and subject headings for depression ("depress*" or "dysthymia" or "mood disorder"; medical subject heading [MeSH] term "Depressive Disorder") in children and adolescents ("youth*," "adolescen*," "child," "pediatric," "paediatric"; MeSH terms "Child," "Child, Preschool" and "Adolescent"). The search included English-language studies involving humans, published from database inception to May 16, 2022. We identified additional sources by examining the references of relevant publications. We included systematic and narrative reviews, randomized controlled trials and cohort studies that addressed aspects of the diagnosis or management of major depressive disorder or persistent depressive disorder among children and adolescents aged 18 years or younger. We also reviewed relevant clinical practice guidelines from Canada, the United States, United Kingdom, Australia and New Zealand.

What is the burden of depressive illness in adolescents?

The prevalence of depression among adolescents increases with age.[4] Before the COVID-19 pandemic, the prevalence of major depressive disorder (MDD) among adolescents was reported to be about 13%–15%.[6,7] A recent meta-analysis found that around 1 in 4 youth had clinically significant depressive symptoms during the COVID-19 pandemic, with higher rates associated with older age and female sex; it also found the prevalence of symptoms to be higher later during the pandemic period.[8]

The onset of depression before adulthood is associated with greater illness severity in adulthood (i.e., increased number of episodes, hospital admissions and risk of self-harm and suicide), poorer physical health outcomes (including obesity, diabetes and cardiovascular disease)[9,10] and social and occupational outcomes.

What are the multifactorial drivers of depression?

Genetic and environmental factors interact with each other in complex pathways to increase risk of, or resilience to, depression among children and adolescents.[11,12] Family history of depression is associated with a three- to fivefold increased risk of depression among older children,[13] and genome-wide association studies have identified numerous loci correlated with MDD.[12] Several mechanisms can be involved in the intergenerational transmission of depression, including inheritance of genes that are associated with psychological traits that may increase depression risk,[14] exposure to parental depression in the postnatal period,[15] adverse childhood experiences[16] and family conflict.[17] Stigma and experiences of bullying have been linked to increased rates of depression among LGBTQ2+ adolescents.[18] Data from the United States suggest that intersectionality between race and gender exacerbates depression.[19]

How is depression diagnosed in children and adolescents?

Diagnostic criteria for MDD and persistent depressive disorder are summarized in Table 1. Compared with adults with depression, children and adolescents may be more likely to present with irritability and labile — rather than low — mood, somatic concerns and social withdrawal.[21,22] Onset of depression before adulthood may also be associated with atypical features such as hypersomnia and increased appetite.[23] Compared with younger children, adolescents are less likely to present with anxiety, somatic symptoms, psychomotor agitation and hallucinations.[24,25]

Risk assessment is a critical component of the assessment of depression and includes review of current suicidal ideation, intent and plan; recent hopelessness, perceived burdensomeness and impulsivity; previous suicide attempts and nonsuicidal self-injury; situational stressors; and protective factors, including supports and future orientation.[2,26,27] Validated scales such as the Columbia Suicide Severity Rating Scale may supplement clinical judgment.[28,29]

Should clinicians screen for adolescent depression?

Although no direct evidence currently indicates that universal screening for MDD in primary care leads to improved outcomes, indirect evidence suggests that treatment of MDD detected through screening is associated with moderate benefit.[30] The United States Preventive Services Task Force (USPSTF) and most clinical practice guidelines (Table 2) recommend screening for depression in primary care for young people aged 12–18 years. In 2005, the Canadian Task Force on Preventive Health Care recommended against routine screening for youth,[39] concluding that more research examining associated risks and benefits was needed; an updated guideline is pending.[47] Screening in this age group may be a reasonable approach, however, when implemented together with adequate systems that ensure accurate diagnosis and appropriate follow-up.[30]

Validated screening tools for adolescent depression are listed in Table 3. Consistent with USPSTF recommendations and guideline appraisal (Table 2),[43] we suggest use of the Patient Health Questionnaire-9 (PHQ-9), the PHQ modified for adolescents (PHQ-A), or the Center for Epidemiologic Studies Depression Scale for Children, all of which are in the public domain.[54] The PHQ-2 (which does not include items related to suicidality) may be appropriate for an initial remote screen, followed by a PHQ-9 in clinic if the initial screen is positive.[34] The same tools may be used for monitoring of treatment response. Further assessment of the patient is required for diagnosis. A collateral history from parents or others able to comment on core symptoms and functioning is helpful.[55] More general tools,

Table 1: Summary of diagnostic criteria for major depressive disorder and persistent depressive disorder*

Diagnosis	Criteria
Major depressive disorder	Two weeks of a persistent change in mood that is either depressed or irritable, or persistent loss of interest or anhedonia, accompanied by at least 3 of the following symptoms of a major depressive episode, present most days: • weight loss (or failure to gain weight) • change in appetite • insomnia or hypersomnia • psychomotor retardation or agitation • fatigue or loss of energy • excessive or inappropriate guilt or feelings of worthlessness • indecisiveness or diminished ability to concentrate • recurrent thoughts of death or suicidal ideation These symptoms result in a change from previous functioning and are not attributable to substances, medications or other disorders.
Persistent depressive disorder	Episode of depressed or irritable mood that persists for at least 1 year, accompanied by at least 2 of the following symptoms, present most days: • hopelessness • insomnia or hypersomnia • hyperphagia or poor appetite • fatigue or low energy • low self-esteem • indecisiveness or poor concentration These symptoms result in a change from previous functioning and are not attributable to substances, medications or other disorders. There may or may not be associated intermittent or persistent major depressive episodes.

*Refer to *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition, Text Revision*[20] for full criteria.

such as the SSHADESS (strengths, school, home, activities, drugs and substance use, emotions, eating, and depression, sexuality and safety) interview,[56] can identify risk factors for mental health conditions, but are not validated as screening tools for psychiatric disorders.

Before assessment, clinicians should review confidentiality rules and limits with the patient and caregivers, emphasizing respect for autonomy and addressing any questions regarding sharing of or access to the patient's medical information. Limits to confidentiality should also be addressed, including situations in which the clinician would be obliged to share information with parents, guardians or other services. The patient and caregiver may be seen together initially and then separately, according to the adolescent's level of comfort. If a patient does not want the caregiver informed of specific details of the assessment, we suggest working collaboratively to understand barriers to disclosure and ways to facilitate sharing of information that may help parents provide support. When safety concerns relevant to management are present and need to be shared with parents, the clinician should inform the young person and involve them in discussion about how this will be done.

What differential diagnoses should be considered?

The differential diagnosis for MDD includes adjustment disorder with depressed mood, sadness or irritability related to situational stressors, persistent depressive disorder (without a history of major depressive episode) and bipolar disorder. Clinicians should consider whether substances and medications are contributing to the presentation. Demoralization and dysphoria can occur secondary to other mental or physical health disorders, or

Table 2: Clinical practice guidelines addressing the assessment or management of depressive disorders among children and youth

Organization	Guideline	Publication year*	AGREE-II score†
American Academy of Pediatrics	Guidelines for adolescent depression in primary care (GLAD-PC) – part I: practice preparation, identification, assessment and initial management[31]	2018	60‡
	Guidelines for adolescent depression in primary care (GLAD-PC) – part II: treatment and ongoing management[32]		
American Academy of Child and Adolescent Psychiatry	Practice parameter for the assessment and treatment of children and adolescents with depressive disorders[33]	2007	55
	Clinical practice guideline for the assessment and treatment of children and adolescents with major and persistent depressive disorders[34]	2022	NA
American Psychological Association	Clinical practice guideline for the treatment of depression across three age cohorts[35]	2019	67‡
Canadian Network for Mood and Anxiety Treatments	Clinical guidelines for the management of adults with major depressive disorder: section 6, special populations: youth, women and the elderly[36]	2016	60‡
Canadian Paediatric Society	Practice point on suicidal ideation and behaviour[37]	2015 (2019)	NA
	Position statement for the use of selective serotonin reuptake inhibitor medications for treatment of child and adolescent mental illness[38]	2013	NA
Canadian Task Force on Preventive Health Care	Screening for depression in primary care: recommendation statement from the Canadian Task Force on Preventive Health Care[39]	2005	NA
National Institute for Health and Care Excellence	Guideline on depression in children and young people: Identification and management[40]	2019	72‡
Royal Australian and New Zealand College of Psychiatrists	Clinical practice guidelines for mood disorders[41]	2020	70‡
United States Preventive Service Task Force	Final Recommendation Statement: Depression in Children and Adolescents: Screening[42]	2016	48

Note: AGREE = Appraisal of Guidelines for Research and Evaluation, NA = not available.
*Original date of publication, with date of update indicated in brackets, if applicable.
†See Yan and colleagues[43] for guideline appraisal using the AGREE II tool.[44]
‡Designated as "recommended" based on Agree-II score.[43] See Bennett and colleagues[45] for an appraisal of earlier versions of several practice guidelines and Duda and colleagues[46] for discussion of the role of critical appraisal of practice guidelines in child and youth mental health.

Table 3: Validated screening tools for depression in children and youth*

Screening tool	Age, yr	Forms	Access
Patient Health Questionnaire (PHQ)-9: Modified for Teens[48]	12–18	Self-report	Public domain; available from the GLAD-PC toolkit at http://gladpc.org/
Center for Epidemiologic Studies Depression Scale for Children (CES-DC)[49]	≥ 6	Self-report	Public domain; available at https://www.aacap.org/App_Themes/AACAP/docs/member_resources/toolbox_for_clinical_practice_and_outcomes/symptoms/ces_dc.pdf
Mood and Feelings Questionnaire[50]	6–19	Self-report	Copyrighted but free for noncommercial use; available at https://devepi.duhs.duke.edu/measures/the-mood-and-feelings-questionnaire-mfq/
		Parent-report	
Revised Children's Anxiety and Depression Scale[51]	8–18	Self-report	Copyrighted but free for noncommercial use; available at https://www.childfirst.ucla.edu/resources
		Parent-report	
Beck Depression Inventory[52]	≥ 13	Self-report	Available for purchase
Child Depression Inventory[53]	7–17	Self-report	Available for purchase
		Parent-report	
		Teacher-report	

*A general list of mental health screening tools and rating scales can be accessed via the Canadian Paediatrics Society (https://cps.ca/en/mental-health-screening-tools).

to psychosocial factors. Bipolar disorder is often initially misidentified as unipolar MDD because the mood episode at onset is frequently a depressive one; it may also be challenging to elicit a history of subtle or short-duration hypomanic symptoms.[36,57] Further risk factors for bipolar disorder are listed in Table 4.

More than 60% of adolescents with MDD have at least 1 comorbid mental health diagnosis,[2] most commonly anxiety disorders, attention-deficit hyperactivity disorder (ADHD), oppositional defiant disorder, conduct disorder and substance use disorders; others include eating disorders, learning disorders and somatic disorders.[64] Youth with chronic medical conditions including chronic pain, neurologic disorders and autoimmune or inflammatory diseases also have higher levels of comorbid depressive symptoms than healthy peers.[56,65,66] Among these youth, symptoms such as fatigue, decreased concentration, sleep and appetite disturbances may overlap with features of depression, making the diagnosis challenging; thoughts of guilt, hopelessness, worthlessness or suicidal ideation raise concern for MDD.[67] A bidirectional relationship is often found between comorbid psychiatric (e.g., ADHD, anxiety, learning disorders) and physical conditions and depression; pre-existing conditions are often predisposing factors for an eventual diagnosis of MDD. Moreover, MDD is frequently an independent risk factor for poor treatment response and increased morbidity of other chronic physical and psychiatric disorders.[68]

Physical health conditions may also mimic primary depressive disorder, including hypothyroidism, anemia, mononucleosis, traumatic brain injury and autoimmune disorders.[33] Physical examination, together with investigations such as complete blood count and thyroid-stimulating hormone levels, are often appropriate to rule out anemia and hypothyroidism. Further laboratory work-up, electrocardiography, electroencephalography and neuroimaging are not generally indicated but may be considered in some circumstances based on history and physical examination.

Table 4: Clinical features of major depressive episodes that may raise the index of suspicion for underlying bipolar disorder and prompt specialist referral

Type	Feature
Symptoms	Presence of mixed symptoms
	Mood lability
	Psychomotor retardation
	Delusions including pathological guilt
	Psychotic symptoms
	Catatonia
Course	Abrupt onset or offset
	Recurrent, shorter episodes
	Frequent episodes
	Treatment resistance
	SSRI-induced mania
Family history	Bipolar disorder
	Psychotic disorder
	Parental illness characteristics (e.g., age at onset, severity)
	Suicide

Note: SSRI = selective serotonin reuptake inhibitor.
Refer to O'Donovan et al. for recent review of bipolar risk in depression,[58] with risk factors also compiled from recent studies.[57,59–63]

How should depression be managed in adolescents?

A multimodal management plan for children and youth with depression begins with psychoeducation and may involve lifestyle management, psychotherapy and medication, in addition to addressing potential contributing factors. Symptom monitoring

during treatment using standardized, validated measures is encouraged (Table 3). Importantly, a suicide risk assessment must be done to ensure appropriateness of an outpatient management plan and facilitate safety planning.

Psychoeducation provides the adolescent and family with an understanding of the factors that may relate to the condition, the diagnosis and the anticipated course of treatment. A shared understanding is essential for engagement in treatment.[2,69] It can be helpful to caregivers even if the youth with depression is reluctant to engage in their own treatment, as these techniques can facilitate problem solving and family communication skills.[34]

Lifestyle measures

Lifestyle interventions include strategies to improve physical activity, dietary patterns and sleep. Systematic reviews of observational studies have noted that unhealthy lifestyle factors are associated with increased depressive symptoms among children and adolescents.[70] Although lifestyle interventions have been endorsed by clinical practice guidelines, particularly with respect to the management of mild-to-moderate MDD, data are less robust than for adults with MDD.[71] Clinicians should exercise caution in overstating the effects of lifestyle interventions as standalone interventions for youth with moderate-to-severe MDD; however, given that effectiveness varies by individual, depressed adolescents frequently feel that they are to blame for their illness, and depressive symptoms (e.g., fatigue, anhedonia, appetite disturbance) are perpetuating factors for unhealthy lifestyles. Further research is needed to better characterize the optimal use of lifestyle interventions, the patient- and disease-specific factors most likely to respond to these strategies and the magnitude of the effect size that adolescents, families and clinicians can expect.

Regular moderate-to-vigorous physical activity has been shown to improve mood in youth.[72,73] Some studies suggest that even short durations of exercise may be effective.[74] The potential benefits of physical activity as standalone interventions are greater when depressive symptoms are mild to moderate in severity. An association between unhealthy dietary patterns and more severe depressive symptoms has been shown in observational studies.[70,75] Randomized controlled trials (RCTs) of dietary interventions for adults with MDD suggest that a diet lower in sugar-sweetened drinks, processed foods and meats, and higher in vegetables, fruit and legumes is associated with lower depressive symptoms.[76]

Bright light therapy has been evaluated in a few small trials involving young patients, and the results suggest a positive effect, particularly for seasonal depression.[77]

Psychotherapy

Cognitive behavioural therapy (CBT) is the psychotherapy with the greatest evidence for efficacy in the treatment of adolescent depression.[78,79] This approach targets the cognitive distortions, negative intrusive thoughts and behavioural manifestations of depression, such as anhedonia and decreased motivation.[34] Adolescents with more severe depressive symptoms, poor coping skills and nonsuicidal self-injury tend to have a less robust response to CBT.[80] Interpersonal therapy, in particular when designed for adolescents, has some evidence for efficacy.[78,81] Interpersonal therapy focuses on the role of interpersonal relationships in depression, aiming to reduce interpersonal stress and improve social functioning.[34] A greater number of studies support CBT and interpersonal therapy delivered individually rather than in a group format.[78] Computer-based CBT or interpersonal therapy has been reported to be as effective as in-person administration,[82] although the broad methodological variety (e.g., videos, text, images, gamification strategies, chats with trained therapists or automated bots) in studies of computer-based therapies makes it a challenge to determine which elements are most important and for whom. Both CBT and interpersonal therapy have also been shown to improve mood among adolescents with subthreshold depressive symptoms, but studies have not been able to show whether progression to full MDD is prevented by these interventions. Involvement of caregivers seems to have a better response than therapies focusing only on the adolescent.[83] Although family therapy, mindfulness-based therapies and short-term psychodynamic therapy may be helpful, the evidence supporting their use is more modest than for CBT or interpersonal therapy.[78,84] Dialectical behavioural therapy has shown promising results, specifically in reducing suicidal ideation and nonsuicidal self-injury among adolescents.[59] Acceptance and commitment therapy, a technique that focuses on acknowledging the painful emotions that come with depression as valid, and on creating strategies to move past them, has been garnering interest recently, but at this point, evidence to support its effectiveness is limited.

Medications

The decision to start antidepressant medication should be made through a collaborative process with the patient and caregivers, taking into account clinical presentation, and after the clinician outlines the range of evidence-based treatment options.[34] Antidepressant medications are recommended for young people with more severe clinical presentations, or in circumstances where psychological therapy is not effective or possible.[34] The risks of pharmacologic therapy should be weighed against those of inadequately treating depression in this vulnerable population.[85] Most clinical guidelines, including the 2019 guideline from the National Institute for Health and Care Excellence in the United Kingdom, recommend initial treatment with psychotherapy only, rather than combined treatment, given the potential adverse effects of medication.[40] Some guidelines suggest trying psychoeducation and lifestyle modifications for 2 weeks, or evidence-based psychotherapies such as CBT or interpersonal therapy for 4–6 sessions, before considering an antidepressant medication.[34,38,40]

Fluoxetine is the first-line medication recommended in most guidelines. A 2020 meta-analysis of RCTs suggested that only fluoxetine plus CBT or fluoxetine alone were more efficacious than placebo and other interventions for youth with depression.[86] Randomized controlled trials evaluating other selective serotonin reuptake inhibitors (SSRIs) have shown similar efficacy to fluoxetine, but discrepant response rates to placebo, suggesting that the identification of fluoxetine as the only effective SSRI may be an artifact of the varied study designs across SSRI trials.[87,88] Modest evidence supports use of sertraline and escitalopram.[37] Most clinical guidelines recommend at least 2 full SSRI trials before other antidepressant classes are considered, given the limited efficacy data and poorer tolerability of other medication classes among adolescents.[88] Fluoxetine is

usually started at 10 mg/d and increased after 1 week to 20 mg/d, and may require 2–6 weeks for positive effects to be noted. The largest RCT of fluoxetine for treatment of MDD among youth showed a number needed to treat of 4 for response (defined as very much improved or much improved on the Clinical Global Impression-Improvement scale) over the first 12 weeks.[89] If fluoxetine is not well tolerated or efficacious, clinicians should consider pharmacokinetics and tolerability when choosing a different SSRI that has some, albeit more modest, evidence for efficacy in adolescent depression (e.g., sertraline, escitalopram). Prescribers should regularly assess clinical response and optimize the SSRI dose as needed and tolerated, with the goal of achieving full symptomatic remission.[90] Patients who do respond well to SSRIs usually experience a gradual improvement of their symptoms, with relatively mild adverse effects that resolve as treatment progresses. Once full remission is achieved, treatment with an SSRI should continue at the therapeutic dosage for at least another 6–12 months before considering a slow taper.

Antidepressant exposure has been associated with an increased risk of suicidal ideation and behaviour in about 2% of young people with depression, particularly during the first few weeks of treatment.[91] Clinicians should discuss these risks with patients and caregivers before starting medication, with consideration that untreated depression is itself a major risk factor for suicide.

Mild gastrointestinal effects are common during the first 4 weeks of treatment, and usually resolve by week 8.[92] Transient insomnia can be managed by taking the medication in the morning.[92] Activation symptoms like jitteriness, restlessness or anxiety may occur early in treatment if the titration is too rapid.[92]

Complementary and alternative medicines are not recommended by current guidelines.[34,40] Preliminary data are promising for St. John's wort and, to a lesser extent, S-adenosylmethionine and 5-hydroxytryptophan.[93] However, studies of these agents have tended to be small or uncontrolled when compared with studies of lifestyle modifications. Adverse effects and drug interactions should be noted; St. John's wort induces the activity of enzymes in the cytochrome P450 family (CYP3A4, CYP2D9 and CYP2C19), making drugs such as oral contraceptives, warfarin, cyclosporin and indinavir less effective. Preparations can vary greatly in quality and content of active ingredients (hypericin and hyperforin), making it challenging to optimize dosing and manage adverse effects.[93]

If patients with MDD do not respond adequately to treatment, it is advisable to revisit the differential diagnosis and consider referral. Specialist support is required for adolescents presenting with acute safety concerns, for complex presentations including symptoms consistent with bipolar disorder and for patients not responding to first-line treatment (Box 2).

Conclusion

Depression is an increasingly common but treatable condition among adolescents. Primary care physicians and pediatricians are well positioned to support the assessment and first-line management of depression in this group, helping patients to regain their health and function. Future research that addresses important clinical questions in the detection and treatment of adolescent depression is needed (Box 3).

Box 2: When to refer to psychiatry or other specialized care

- Diagnostic clarification, particularly for patients with concern for
  - Psychotic features
  - Hypomania or mania
  - Comorbidities affecting diagnosis and treatment (e.g., substance use, trauma, autism spectrum disorder, other neurodevelopmental disorders)
- Suicidal or homicidal behaviour, or acute safety concerns
- Severe functional impairment or psychosocial stressors
- Treatment nonresponse or serious adverse effects of treatment
- Recurrent or persistent depression
- Management of comorbid psychiatric disorders that are not responding to treatment

Box 3: Unanswered questions

- What are the differential impacts of the COVID-19 pandemic on prevalence of depressive disorders among subgroups of children and youth in Canada?
- Does screening for depression in primary care and school settings lead to improved outcomes?
- How can lifestyle interventions be used most effectively to improve depressive symptoms?
- What patient, family and treatment factors affect outcomes of selective serotonin reuptake inhibitors, psychotherapy and combination treatments?

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